Perivascular support of human hematopoietic stem/progenitor cells.

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Public Summary:
Mesenchymal stem/stromal cells (MSCs) are multipotent progenitors with the ability to sustain hematopoietic cells. Recent findings have showed that MSCs are functionally heterogeneous, i.e. constituted by different subsets of cells with different functions. The identity of the subset of human MSCs involved in hematopoietic support has been so far unknown. In the present study, Corselli et al. identified for the first time CD146+ perivascular cells as the subset of MSCs able to maintain hematopoietic stem and progenitor cells (HSPCs) after ex vivo culture. The authors first demonstrate that CD146+ perivascular cells surround the blood vessels present in human bone marrow and fat. They also show that these cells express markers of the perivascular hematopoietic niche (nestin, CXCL12, leptin receptor), as previously reported in mouse bone marrow. CD146+ cells purified to homogeneity via FACS sorting promoted superior HSPC survival and prevented differentiation toward myeloid or lymphoid lineages as compared to unfractionated and heterogeneous MSCs. Furthermore, only CD146+ could maintain HSPCs with the ability to repopulate the hematopoietic system of immunodeficient mice. Interestingly, CD146+ cells able to support HSPCs were also found in human adipose tissue, an abundant and convenient source of stem cells.

Scientific Abstract:
Hematopoietic stem and progenitor cells (HSPCs) emerge and develop adjacent to blood vessel walls in the yolk sac, aorta-gonad-mesonephros region, embryonic liver, and fetal bone marrow. In adult mouse bone marrow, perivascular cells shape a "niche" for HSPCs. Mesenchymal stem/stromal cells (MSCs), which support hematopoiesis in culture, are themselves derived in part from perivascular cells. In order to define their direct role in hematopoiesis, we tested the ability of purified human CD146(+) perivascular cells, as compared with unfractionated MSCs and CD146(-) cells, to sustain human HSPCs in coculture. CD146(+) perivascular cells support the long-term persistence, through cell-to-cell contact and at least partly via Notch activation, of human myelolymphoid HSPCs able to engraft primary and secondary immunodeficient mice. Conversely, unfractionated MSCs and CD146(-) cells induce differentiation and compromise ex vivo maintenance of HSPCs. Moreover, CD146(+) perivascular cells express, natively and in culture, molecular markers of the vascular hematopoietic niche. Unexpectedly, this dramatic, previously undocumented ability to support hematopoietic stem cells is present in CD146(+) perivascular cells extracted from the nonhematopoietic adipose tissue.